EXHIBIT A20

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An Update of a Mortality Study of Talc Miners and Millers in Italy

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Background *While talc containing asbestiform fibers is considered a human carcinogen, only limited animal and human data are available on non-asbestiform talc. To provide further evaluation on the issue, we updated the analysis of an Italian cohort of talc miners and millers in Val Chisone; talc found here is free from asbestiform fibers.*

Methods *The cohort was comprised of 1,795 men who had worked for at least 1 year in the mine and/or in the factory between 1946 and 1995. Vital status and death certificates were obtained from registration offices in the municipality of death or of birth. Employment, termination of employment, and detailed job history were obtained from personnel records at the plant.*

Results *No excess was found for total cancer mortality, nor mortality for lung cancer. No case of mesothelioma was reported. There was a significant excess mortality from non-neoplastic respiratory diseases (SMR 228.2, 95% CI 190.2–271.5). Mortality excess for non-neoplastic respiratory diseases was mainly due to silicosis.*

Conclusions *This study provides additional support for an association between talc in mining and milling and non-neoplastic respiratory diseases, while showing no significant excess risk for lung cancer and mesothelioma. The results also provide additional information of interest to evaluate the potential association between silica and lung cancer.*
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***KEY WORDS:** cohort mortality study; talc; silica; miners and millers; mesothelioma; lung cancer*

INTRODUCTION

Talc is a silicate with a lamellar structure that can be contaminated with other minerals including asbestiform fibers. That is the reason why a former definition was "fibrous talc."

While talc containing asbestiform fibers is considered a human carcinogen [IARC, 1997], only limited animal and human data are available on the potential carcinogenic effect of non-asbestiform talc.

Lung cancer and pleural mesothelioma have been the main sites considered in occupational cohort studies of non-asbestiform talc. Of these, three showed no excess risk. A historical cohort study of 1992 talc miners and millers in Italy followed between 1946 and 1974 showed a standardized mortality ratio (SMR) of 47 among miners and 66 among millers for lung cancer, and no cases of pleural mesothelioma

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[Rubino et al., 1976, 1979]. A study of 392 workers from Vermont, US [Selevan et al., 1979] and one of 389 workers from Norway [Wergeland et al., 1990] found no excess risk for millers, but some excess for miners, which may however be related to radon exposure. A study of 2,055 pottery workers from the US, in contrast, showed an excess lung cancer mortality (relative risk (RR): 2.5) among workers exposed to non-fibrous talc plus silica [Thomas and Stewart, 1987].

To provide further evaluation on the issue, we updated the analysis of the Italian cohort of talc miners and millers in Val Chisone, Turin [Rubino et al., 1976, 1979], in which the talc was free from asbestiform fibers [Verdel et al., 1983; Parkes, 1994]. The large size of the cohort and the uniquely long follow-up allow separate analyses by job title, besides detailed considerations of latency and other time factors. The presence of data on exposure levels between 1946 and 1975 [Rubino et al., 1976] and between 1990 and 1995 allow further considerations.

SUBJECTS AND METHODS

The cohort was comprised of 1,974 men who had worked for at least 1 year in the mine and/or in the factory between 1946 and 1995. After exclusion of 179 men with no follow-up information, the analyses were based on 1,795 subjects (90.9% of the total).

Dates of birth, employment and termination of employment, the last known address and detailed job history were obtained from personnel records at the plant. No information was available on smoking habits. Death certificates were obtained from registration offices in the municipality of death.

Further verification of vital status was obtained from registries of current residence.

For the present analysis, the follow-up began 1 January 1946 and ended at 31 December 1995. A total of 880 deaths and 50,701 man-years were documented.

DATA ANALYSIS

The expected number of deaths from all causes, selected cancer sites and other selected non-neoplastic conditions were computed using national and regional death rates for each 5 year calendar period and age group. Regional rates were provided by the Regional Cancer Register of Piedmont for the period 1970–95, and national death rates were used before 1970. Rates for the early 1950s were applied to the period 1946–49. No regional rates for cancers of the oral cavity and esophagus and for suicides were available; national rates were also used after 1970.

We computed SMRs (SMR = observed/expected × 100) and the corresponding 95% confidence intervals (CI) [Breslow and Day, 1987]. We also computed observed and expected numbers by year of first employment, duration of employment, and type of job (miners and millers). Miners (n = 1,244) were all men who worked in the mine only, or with mixed exposure in the mine and in the plant. The job category defined as "millers" comprised millers and other workers of the plant only (n = 551).

RESULTS

Table I gives observed and expected death and the corresponding SMR for all causes of death, selected cancer sites and other major non-neoplastic causes of death. Total mortality was significantly higher than expected (880 observed vs. 735 expected, SMR 119.7, 95% CI 111.9–127.9).

There was no excess mortality for all cancers (185 observed, 186.5 expected, SMR 99.2, 95% CI 85.4–114.5). No deaths were seen from pleural or peritoneal mesotheliomas, and there was no excess deaths from lung cancer (44 observed, 46.9 expected, SMR 93.8, 95% CI 68.1–125.9).

A significant excess mortality was found from oral cavity cancer (31 observed vs. 6 expected, SMR 514.4, 95% CI 349.4–730.1) and esophageal cancer (10 observed,

TABLE I. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946–1995

	OBS	EXP	SMR	95% CI	
All causes	880	735	**119.7**	111.9	127.9
All cancers	185	186.5	99.2	85.4	114.5
Oral cavity	31	6	**514.4**	349.4	730.1
Esophagus	10	4.7	**212.9**	101.9	391.6
Stomach	31	26.8	115.5	78.5	164
Intestines	13	19.9	65.4	34.8	111.8
Liver and gall bladder	10	8.6	116.6	55.8	214.5
Pancreas	7	6.2	112.7	45.2	232.3
Peritoneum	0	0.9	0	0	393.8
Larynx	8	7	115	49.5	226.7
Lung	44	46.9	93.8	68.1	125.9
Pleura	0	1.8	0	0	206.9
Connectival sarcoma	1	0.2	469	6.1	2609.3
Skin	3	1.6	183.1	36.8	535
Prostate	6	10.5	57.3	20.9	124.7
Bladder	1	8.7	11.5	0.2	64
Kidney	1	2.9	33.9	0.4	188.9
Non Hodgkin lymphomas	2	2.9	69.7	7.8	251.8
Hodgkin's disease	0	1.8	0	0	204.7
Leukemia	5	7	71.7	23.1	167.4
Diabetes	5	11.0	45.3	14.6	105.8
Cardiovascular diseases	288	309.2	93.2	82.7	104.6
Ischemic heart disease	88	101.6	86.6	69.5	106.7
Cerebrovascular disease	60	90.2	66.5	50.8	85.7
Respiratory tract diseases	127	55.7	**228.2**	190.2	271.5
Digestive tract diseases	79	55.5	**142.2**	112.6	177.3
Cirrhosis	55	31.2	**176.3**	132.8	229.4
Injuries	49	49.2	99.6	73.7	131.7

4.7 expected, SMR 212.9, 95% CI 101.9–391.6). There was a non-significant excess mortality from stomach cancer (31 observed, 26.8 expected, SMR 115.5, 95% CI 78.5–164).

With reference to non-neoplastic causes of death, there was a significant excess mortality from respiratory tract diseases (127 observed, 55.7 expected, SMR 228.2, 95% CI 190.2–271.5), from digestive tract diseases (79 observed, 55.5 expected, SMR 142.2, 95% CI 112.6–177.3), and from liver cirrhosis (55 observed, 31.2 expected, SMR 176.3, 95% CI 132.8–229.4). Mortality excess for non-neoplastic respiratory diseases was mainly due to silicosis (62 deaths). In fact, excluding silicosis from deaths for non-malignant respiratory disease, the SMR was 116.6 (95% CI 97.1–138.5). The SMR was 93.2 for cardiovascular disease, 86.6 for ischemic heart disease, 66.5 for cerebrovascular disease. For 62 subjects, the cause of death was unknown or undefined.

The excess mortality from cancers of the oral cavity and esophagus, digestive tract disease, and liver cirrhosis was similar for miners and millers. Conversely the excess in all causes mortality and particularly respiratory tract diseases were confined to miners only.

Table II gives corresponding stratified analysis for miners and millers.

The excess risk for miners is attributable to silicosis (58 silicosis observed in miners compared to 4 in millers). No increase in mortality from lung cancer was seen in miners or millers.

Table III shows mortality by duration of exposure. For lung cancer, no significant increase in mortality was found in the four duration levels (less than 10 years—SMR 135.8, between 10 and 19 years—SMR 66.7, between 20 and 29 years—SMR 94.1, over 30 years—SMR 73.2). For oral cavity cancer, the SMR was significantly elevated in the exposure category under 20 years and over 30 years, and for esophageal cancer a significant SMR was seen in the group between 10 and 19 years of exposure, in the absence, however, of any trend in risk with duration. The excess in

TABLE II. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946–1995 by Job Category

	Miners					Millers				
	OBS	EXP	SMR	95% CI		OBS	EXP	SMR	95% CI	
All causes	590	466.8	**126.4**	116.4	137	290	268.3	108.1	96	121.3
All cancers	130	120.6	107.8	90.1	128	55	65.6	83.4	62.8	108.6
Oral cavity	24	3.9	**611.8**	391.8	910.3	7	2.1	**332.7**	133.3	685.6
Esophagus	7	3	231.9	92.9	477.8	3	1.7	178.8	35.9	522.5
Stomach	20	16.8	119.2	72.8	184.1	11	10.1	109.4	54.5	195.7
Intestines	11	12.9	85.5	42.6	152.9	2	7	28.5	3.2	102.8
Liver and gall bladder	4	5.4	73.7	19.8	188.6	6	3.1	190.8	68.7	415.3
Pancreas	4	4.1	98.7	26.5	252.6	3	2.2	139.2	28	406.7
Peritoneum	0	0.6	0	0	599.6	0	0.3	0	0	1147.1
Larynx	7	4.5	154.1	61.7	317.6	1	2.4	41.4	0.5	230.6
Lung	33	30.9	106.7	73.4	149.9	11	16	68.8	34.3	123
Pleura	0	1.2	0	0	312	0	0.6	0	0	614.6
Connectival sarcoma	1	0.1	699.2	9.1	3890.3	0	0.1	0	0	5224.2
Skin	2	1.1	188.2	21.1	679.4	1	0.6	173.8	2.3	966.7
Prostate	3	6.5	46	9.2	134.4	3	4	75.3	15.1	220.1
Bladder	0	5.6	0	0	65.9	1	3.1	31.9	0.4	177.5
Kidney	1	2.2	46.3	0.6	257.7	0	1.1	0	0	327.2
Non Hodgkin lymphomas	0	1.9	0	0	192.9	2	1	206.9	23.2	747.1
Hodgkin's disease	0	1.2	0	0	302.6	0	0.6	0	0	632.8
Leukemias	4	4.6	87.8	23.6	224.7	1	2.4	41.4	0.5	230.5
Diabetes	2	7	28.7	3.2	103.5	3	4.1	74	14.9	216.2
Cardiovascular diseases	177	192.8	91.8	78.8	106.4	111	116.4	95.4	78.5	114.9
Ischemic heart disease	56	64.7	86.5	65.3	112.3	32	36.9	86.8	59.4	122.6
Cerebral vasculopathy	42	55.5	75.7	55.5	102.3	18	34.7	51.9	30.7	82
Respiratory tract diseases	105	34.4	**305.2**	249.6	369.5	22	21.3	103.5	64.8	156.7
Digestive tract diseases	50	36	**138.9**	103.1	183.1	29	19.5	148.4	99.4	213.2
Cirrhosis	37	20.5	**180.3**	127	248.6	18	10.7	168.4	99.8	266.2
Injuries	34	33.2	102.4	70.9	143.1	15	16	93.8	52.5	154.7

TABLE III. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946–1995 by Duration of Exposure

	<10 years (n = 519)				10–19 years (n = 421)				20–29 years (n = 504)				≥30 years (n = 351)			
	OBS	SMR	95% IC		OBS	SMR	95% IC		OBS	SMR	95% IC		OBS	SMR	95% IC	
All causes	212	**134.7**	117.2	154.1	221	**138.2**	120.6	157.7	300	**112.6**	100.2	126.1	147	97.2	82.1	114.2
All cancers	47	113.6	83.4	151.1	50	130.6	96.9	172.2	53	80.7	60.4	105.5	35	85	59.2	118.3
Oral cavity	10	**713.5**	341.6	1312.2	11	**846.6**	422.0	1514.9	5	244	78.6	569.4	5	**391.6**	126.2	913.8
Esophagus	2	198.6	22.3	717.1	4	**399.1**	107.4	1021.9	4	241.3	64.9	617.7	0	0	0	356.3
Stomach	4	77.3	20.8	197.9	9	141.7	64.7	269.1	10	101.2	48.4	186.1	8	147.4	63.5	290.5
Intestines	3	70.1	14.1	204.9	4	110.0	29.6	281.6	3	41.4	8.3	120.9	3	63.5	12.8	185.5
Liver and gall bladder	2	110.4	12.4	398.7	5	247.7	79.8	578.1	2	66.7	7.5	240.7	1	57.3	0.7	319
Pancreas	0	0	0	258.0	3	245.0	49.2	715.8	0	0	0	1170.6	0	0	0	1899.3
Peritoneum	0	0	0	1598.4	0	0	0	1875.2	2	93.4	10.5	337.1	2	140.8	15.8	508.3
Larynx	2	126.6	14.2	457.1	0	0	0	256.3	5	207.3	66.8	483.8	1	65.3	0.9	363.2
Lung	15	135.8	75.9	223.9	6	66.7	24.4	145.3	15	94.1	52.6	155.2	8	73.2	31.5	144.2
Pleura	0	0	0	857.6	0	0	0	1195.2	0	0	0	600.7	0	0	0	858.4
Skin	0	0	0	902.1	2	545.8	61.3	1970.7	1	183.3	2.4	1019.7	0	0	0	1147.6
Connectival sarcoma	0	0	0	6222.6	0	0	0	8646.7	0	0	0	5460	1	2238.1	29.3	12452.4
Prostate	0	0	0	199.8	1	50.7	0.7	281.8	2	47.9	5.4	173	3	119	23.9	347.6
Bladder	1	57.3	0.7	318.6	0	0	0	227.4	0	0	0	112.7	0	0	0	175.9
Kidney	0	0	0	461.5	0	0	0	571.8	1	91.3	1.2	507.8	0	0	0	490.5
Non Hodgkin lymphomas	0	0	0	475.4	1	161.3	2.1	897.2	1	109.6	1.4	609.6	0	0	0	651.2
Hodgkin's disease	0	0	0	632.6	0	0	0	771.9	0	0	0	728.1	0	0	0	1572.6
Leukemias	3	175.9	35.4	514.0	1	69.6	0.9	387.0	0	0	0	153.5	1	69.6	0.9	387
Diabetes	1	46.1	0.6	256.8	1	45.6	0.6	253.7	3	72.5	14.6	211.7	0	0	0	145
Cardiovascular diseases	66	113.4	87.7	144.3	70	107.1	83.5	135.3	108	91	74.6	109.9	44	65.7	47.8	88.2
Cerebral vasculopathy	11	69.2	34.5	123.9	13	68.6	36.5	117.3	24	67.5	43.2	100.4	12	60.7	31.3	106.1
Respiratory tract diseases	23	**225.3**	142.7	338.0	27	**223.3**	147.1	324.9	53	**246**	184.3	321.8	24	**203.1**	130.1	302.2
Digestive tract diseases	18	139.0	82.4	219.8	22	**174.7**	109.4	264.4	22	114.3	71.6	173	17	158.2	92.1	253.3
Cirrhosis	13	173.6	92.4	296.9	17	**250.1**	145.6	400.4	15	140.6	78.7	232	10	159.9	76.6	294.1
Injuries	18	110.6	65.5	174.8	14	115.9	63.3	194.4	11	79.1	39.4	141.5	6	86.7	31.7	188.8
Suicide	2	88.4	9.9	319.2	6	**324.8**	118.6	706.9	2	93.8	10.5	338.6	2	182.2	20.5	657.9

mortality from non-neoplastic respiratory disease was increased in subsequent duration exposure groups, again in the absence of a clear trend of increasing risk with duration. Moreover, there was no consistent duration-risk relation when the analysis was restricted to miners only.

The duration of exposure for total mortality and selected causes of death is considered in Table IV for miners only. The SMR for the longest category (>20 years) were 112.8 for all causes, 91.6 for all cancers, 323.2 for oral cancer, 173.6 for esophageal cancers, 95.9 for lung cancer, and 322.9 for non-neoplastic respiratory diseases. A direct trend in risk with exposure was observed only for non-neoplastic respiratory diseases.

Table V considers the role of time since first exposure (latency) for the same causes of deaths. For the longest latency level, the SMR was 111.1 for all causes, 92.1 for all cancers, 481.7 for oral cancer, 69.1 for esophageal cancer, 90.8 for lung cancer, and 242.4 for non-neoplastic respiratory diseases. Again a direct trend in risk with time from first exposure was observed only for non-neoplastic respiratory diseases.

DISCUSSION

In this cohort, there was an excess total mortality due chiefly to non-neoplastic respiratory diseases (mainly classified as silicosis), liver cirrosis, other digestive tract diseases, and suicides. Furthermore, a non-negligible number of deaths (7%) was for unknown cause. Consequently, assuming a non-differential distribution, the SMR for various causes of deaths may also be somewhat underestimated. The potential error due to the use of national rates is in contrast small, since rates for Piedmont were similar to national ones for most diseases considered [Cislaghi et al., 1986].

Our study found no relation between occupational exposure to non-asbestiform talc and risk of mesothelioma and lung cancer. This finding was common to both millers and miners. Miners were also exposed to quartz, radon, and to

TABLE IV. Total Mortality and Selected Causes of Death by Duration of Exposure for Miners Only

	<10 years				10–20 years				>20 years			
	OBS	SMR	95% CI		OBS	SMR	95% CI		OBS	SMR	95% CI	
All causes	144	**145.4**	122.6	171.2	150	**142.4**	120.5	167.1	296	**112.8**	100.3	126.4
All cancers	37	136.6	96.2	188.3	30	121.4	81.9	173.3	63	91.6	70.3	117.1
Oral cavity	9	**967.2**	441.3	1836.2	8	**967.6**	416.6	1906.7	7	**323.2**	129.5	666.0
Esophagus	2	306.7	34.4	1107.4	2	313.3	35.2	1131.1	3	173.6	34.9	507.1
Stomach	2	63.9	7.2	230.6	5	123.0	39.6	287.1	13	135.7	72.2	232.0
Intestines	3	106.9	21.5	312.5	4	166.9	44.9	427.4	4	52.2	14.0	133.6
Larynx	2	190.8	21.4	689.0	0	0	0	402.2	5	193.7	62.4	452.0
Lung	11	147.0	73.3	263.0	5	87.5	28.2	204.1	17	95.9	55.9	153.6
Cardiovascular diseases	43	123.6	89.4	166.5	45	104.1	75.9	139.3	89	77.5	62.3	95.4
Cerebral vasculopathy	7	75.9	30.4	156.5	10	79.7	38.2	146.6	25	74.1	48.0	109.4
Respiratory tract diseases	17	**284.8**	165.8	455.9	22	**275.1**	172.4	416.6	66	**322.9**	249.7	410.9
Digestive tract diseases	11	130.5	65.0	233.4	15	**182.6**	102.1	301.3	24	124.0	79.4	184.5
Cirrhosis	9	179.6	81.9	340.9	12	**274.0**	141.4	478.7	16	143.8	82.2	233.6
Injuries	12	106.2	54.8	185.5	11	134.0	66.8	239.8	11	80.3	40.1	143.8
Suicide	1	64.2	0.8	357.0	5	**407.6**	131.4	951.2	3	140.5	28.2	410.6

diesel exaust (this last exposure was confined to a short period of time, since 1991). Our results strengthen previous findings on the absence of a major role of non-asbestiform talc in inducing mesothelioma and lung cancer [Rubino et al., 1976, 1979; Leophonte, 1983; Rubino, 1983; Wergeland et al., 1990]. A recent study by Wild et al. [2002] is consistent with our results, since the authors did not find any lung cancer excess mortality from talc exposure.

The results support therefore that excess mortality from mesothelioma and lung cancer can be attributed to asbestiform fibers contained in talc exposure [Kleinfeld et al., 1974; Brown, 1979; Vianna, 1981].

A significant excess mortality from non-malignant respiratory diseases was found in miners only. This observation had already been made by Rubino et al. [1976, 1979] in previous follow-up of the same cohort, and was attributed to the high frequency of silicosis as a cause of death in this cohort. This can be explained by the mixed exposure (including a certain amount of inhalable silica particles) that took place in the past, when rock drilling activity was frequent and technical prevention means had not yet been introduced. Before 1950, dry drilling was still in use and forced ventilation system (FVS) had yet to come; since 1950 wet drilling was introduced and more widely applied in the following years, FVS was introduced between 1958 and 1959 and completed in 1963. Therefore the exposure levels of total respirable dust have been progressively decreasing from 1950 to 1995 (from 100 to 1000 MPPCF—million particles per cubic foot before 1955 to less than 10 MPPCF between 1960 and 1975 [Rubino et al., 1976]). In the last years, exposure levels to talc dusts were monitored and the values in the mine were between 0.5 and 2.5 mg/m^3, mean 1.1 mg/m^3 for respirable fraction and 0.3–2.0 mg/m^3, mean 1.0 mg/m^3 for talc alone. There was a remarkable difference in the amount of free silica in air dust, respectively, in mines and mills and within the mine jobs between drilling and other operations. This was mainly due to the high content of quartz in footwall rocks, as opposed to the absence of free silica in talc minerals. In spite of such an exposure to silica particles, no excess lung cancer was observed in this cohort.

Together with other recent reports, including experimental and epidemiological data evaluations [Chan et al., 2000; Hessel et al., 2000; Soutar et al., 2000; Carta et al., 2001; Cocco et al., 2001], the present study provides additional information of interest to further evaluate the association between silica and lung cancer [IARC, 1997; Steenland et al., 2001].

Combined exposure to talc and asbestos has been associated to gastric cancer risk in one German study of 11,633 rubber workers, with a significant RR of 2.3 [Straif et al., 2000]. The RR for lung cancer was 1.7. However we did not find any significant excess mortality for those cancers.

The significant excess mortality from oral cavity and esophageal cancers is likely due to alcohol consumption and cigarette smoking [La Vecchia et al., 1986; Franceschi et al., 1990]. Elevated alcohol drinking in this cohort is also suggested by the excess mortality from liver cirrosis [Corrao et al., 1998].

CONCLUSIONS

In conclusion, no association was found between exposure to talc containing no asbestos fibers and lung cancer or pleural mesothelioma. An excess mortality from alcohol

TABLE V. Total Mortality and Selected Causes of Death by Time Since First Exposure (Latency) for Miners and Millers

	<20 years				20–30 years				>30 years			
	OBS	SMR	95% CI		OBS	SMR	95% CI		OBS	SMR	95% CI	
All causes	154	**129.6**	109.9	151.7	215	**137.7**	119.9	157.4	511	**111.1**	101.7	121.1
All cancers	29	112.2	75.1	161.2	46	111.4	81.5	148.6	110	92.1	75.7	111.0
Oral cavity	7	**741.1**	296.9	1526.9	7	**450.7**	180.6	928.6	17	**481.7**	280.4	771.3
Esophagus	2	304.6	34.2	1099.8	6	**521.0**	190.3	1134.1	2	69.2	7.8	250.0
Stomach	3	61.7	12.4	180.2	8	117.0	50.4	230.6	20	132.1	80.7	204.1
Intestines	2	118.9	13.3	429.2	2	57.4	6.4	207.2	9	61.1	27.9	116.0
Liver and gall bladder	3	190.6	38.3	557.0	3	136.1	27.4	397.8	4	83.4	22.4	213.5
Pancreas	2	277.9	31.2	1003.4	1	75.9	1.0	422.5	4	95.9	25.8	245.5
Peritoneum	0	0	0	2153.3	0	0	0	1647.3	0	0	0	681.1
Larynx	1	96.0	1.3	533.9	2	114.5	12.9	413.3	5	120.0	38.7	280.1
Lung	6	107.6	39.3	234.2	10	95.2	45.6	175.2	28	90.8	60.3	131.2
Pleura	0	0	0	2325.3	0	0	0	1085.7	0	0	0	287.3
Skin	0	0	0	1190.2	0	0	0	937.5	3	319.5	64.2	933.6
Connectival sarcoma	0	0	0	1048.5	0	0	0	8013.8	1	754.9	9.9	4200.0
Prostate	0	0	0	691.1	0	0	0	229.9	6	71.6	26.1	155.9
Bladder	0	0	0	501.1	0	0	0	231.5	1	15.7	0.2	87.2
Kidney	0	0	0	906.7	0	0	0	522.9	1	46.0	0.6	256.0
Non Hodgkin lymphomas	1	167.9	2.2	934.3	0	0	0	573.5	1	61.3	0.8	340.8
Hodgkin's disease	0	0	0	493.7	0	0	0	768.8	0	0	0	641.2
Leukemias	0	0	0	285.7	2	138.8	15.6	501.2	3	70.7	14.2	206.4
Diabetes	1	91.1	1.2	506.7	0	0	0	170.6	4	51.4	13.8	131.6
Cardiovascular diseases	32	90.5	61.9	127.8	72	117.6	92.0	148.1	184	86.6	74.5	100.0
Cerebral vasculopathy	7	78.9	31.6	162.6	15	87.1	48.7	143.6	38	59.3	42.0	81.4
Respiratory tract diseases	11	147.6	73.4	263.6	26	**234.8**	153.4	344.1	90	**242.4**	194.9	298.0
Digestive tract diseases	16	136.0	77.7	220.9	26	**182.7**	119.3	267.7	37	125.2	88.2	172.6
Cirrhosis	11	180.8	90.1	323.5	23	**265.8**	168.4	398.8	21	127.5	78.9	195.0
Injuries	25	134.6	87.1	198.6	8	70.1	30.2	138.1	16	83.3	47.6	135.3
Suicide	6	233.6	85.3	508.5	2	107.8	12.1	389.2	4	137.2	36.9	351.3

related cancers and from other non-malignant disease relative to alcohol was found. Mortality from non-malignant respiratory diseases was increased only in miners, and this excess can be attributed to a mixed exposure to quartz in past years. Furthermore our mortality data from silicosis in miners, in the absence of an excess mortality from lung cancer, do not support the hypothesis of an association between silica exposure, silicosis, and the development of lung cancer.

REFERENCES

Breslow NE, Day NE. 1987. Statistical methods in cancer research. Volume II—The design and analysis of cohort studies. IARC Sci Publ 82, 406 p.

Brown DP. 1979. Mortality patterns among miners and millers occupationally exposed to asbestiform talc. In: Lemen R, Dement JM, editors. Dust and Disease. Park Forest South, IL: Pathotox, p 317–324.

Carta P, Aru G, Manca P. 2001. Mortality from lung cancer among silicotic patients in Sardinia—An update study with 10 more years of follow up. Occup Environ Med 58(12):786–793.

Chan CK, Leung CC, Tam CM, Yu TS, Wong TW. 2000. Lung cancer mortality among a cohort of men in a silicotic register. J Occup Environ Med 42(1):69–75.

Cislaghi C, Decarli A, La Vecchia C, Laverda N, Mezzanotte G, Smans M. 1986. Dati, indicatori e mappe di mortalità tumorale. Italia 1975/1977 (Data, indicators and map of cancer mortality. Italy 1975/1977). Bologna: Pitagora Editrice Bologna. (in Italian)

Cocco P, Rice CH, Chen JQ, McCawley MA, McLaughlin JK, Dosemeci M. 2001. Lung cancer risk, silica exposure, and silicosis in Chinese mines and pottery factories—The modifying role of other workplace lung carcinogens. Am J Ind Med 40(6):674–682.

Corrao G, Zambon A, Torchio P, Arico S, La Vecchia C, Di Orio F. 1998. Attributable risk for symtomatic liver cirrhosis in Italy. J Epatol 28:608–614.

Franceschi S, Talamini R, Barra S, Baron AE, Negri E, Bidoli E, Serraino D, La Vecchia C. 1990. Smoking and drinking in relation to

cancers of the oral cavity, pharynx, larynx and esophagus in Northern Italy. Cancer Res 50:6502–6507.

Hessel PA, Gamble GF, Gee JB, Gibbs G, Green FH, Morgan WK, Mossman BT. 2000. Silica, silicosis, and lung cancer: A response to a recent working group report. J Occup Environ Med 42(7):704–720.

International Agency for Research on Cancer. 1997. Silica, some silicates, coal, dust and para aramid fibrils. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon. Volume 68, 506 p.

Kleinfeld M, Messite J, Zaki MH. 1974. Mortality experience among talc workers—A follow up study. J Occup Med 16(5):345–349.

La Vecchia C, Decarli A, Mezzanotte G, Cislaghi C. 1986. Mortality from alcohol related diseases in Italy. J Epidemiol Community Health 40:257–261.

Leophonte P. 1983. Mortality of talc workers in France—Retrospective epidemiological study. Rev Fr Mal Respir 11:489–490.

Parkes WR. 1994. Occupational lung disorders. 3rd ed. London: Butterworths, 892 p.

Rubino GF. 1983. Talc millers mortality study. Proceedings 6th Industrial Hygiene Meeting. Rome, p 60–65.

Rubino GF, Scansetti G, Piolatto PG, Romano C. 1976. Mortality study of talc miners and millers. J Occup Med 18:186–193.

Rubino GF, Scansetti G, Piolatto G, Gay G. 1979. Mortality and morbidity among talc miners and millers in Italy. In: Lemen R, Dement JM, editors. Dust and Disease. Illinois, USA: Pathotox, p 357–363.

Selevan SG, Dement JM, Wagoner JK, Froines JR. 1979. Mortality patterns among miners and millers of non-asbestiform talc: Preliminary report. In: Lemen R, Dement JM, editors. Dust and Disease. Illinois, USA: Pathotox, p 378–388.

Soutar CA, Robertson A, Miller BG, Searl A, Bignon J. 2000. Epidemiological evidence on the carcinogenicity of silica—Factors in scientific judgement. Ann Occup Hyg 44(1):3–14.

Steenland K, Mannetje A, Boffetta P, Stayner L, Attfield M, Chen J, Dosemeci M, DeKlerk N, Hnizdo E, Koskela R, Checkoway H. 2001. Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: An IARC multicentre study. Cancer Causes Control 12:773–784.

Straif K, Keil U, Taeger D, Holthenirch D, Sun Y, Bungers M, Weiland SK. 2000. Exposure to nitrosamines, carbon black, asbestos, and talc and mortality from stomach, lung, and laryngeal cancer in a cohort of rubber workers. Am J Epidemiol 152(4):297–306.

Thomas TL, Stewart PA. 1987. Mortality from lung cancer and respiratory disease among pottery workers exposed to silica and talc. Am J Epidemiol 125:35–43.

Verdel U, Sperduto B, Perrone GB, Laurini C. 1983. Talchi dei principali depositi mediterranei (Francia, Italia, Spagna) e minerali che li accompagnano (Talc varieties in the main Mediterranean deposits (France, Italy and Spain), and contaminating minerals). Riv Inf Mal Prof 6:725–736. (in Italian)

Vianna NJ. 1981. Malignant mesothelioma—Epidemiologic patterns in New York State. NY State J Med 735–738.

Wergeland E, Andersen A, Bärheim A. 1990. Morbidity and mortality in talc-exposed workers. Am J Ind Med 17:505–513.

Wild P, Leodolter K, Refregier M, Schmidt H, Zidek T, Haidinger G. 2002. A cohort mortality and nested case-control study of French and Austrian talc workers. Occup Environ Med 59(2):98–105.